UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,158	03/28/2001	Shouji Furusako	1110-0284P	5167

2292 7590 10/28/2003

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 10/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/806,158	Applicant(s) FURUSAKO et al.
	Examiner James L. Grun, Ph.D.	Art Unit 1641

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-14 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-14 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 1, 8, 9
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1641.

The disclosure is objected to because of the following informalities: the specification is replete with grammatical, idiomatic, and spelling errors and should be carefully revised. For example: "low molecular soluble" should be --low molecular weight soluble--; "high molecular soluble" should be --high molecular weight soluble--; page 1, Title, "PROTAINS" should be --PROTEINS--; page 4, line 12, --phosphatidylserine-- should be recited; page 13, line 1, --measurement-- should be recited; page 61, line 19, --prepared-- should be recited; etc. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

The specification is objected to and claims 9 and 11-14 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to

provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are: (1) known and readily available to the public; (2) reproducible from the written description; or, (3) deposited in compliance with the criteria set forth in 37 CFR §§ 1.801-1.809.

It is unclear if cell lines which produce antibodies having the exact chemical identity and properties of the antibodies designated FERM BP-7295 or FERM BP-7296 are known and publicly available, or can be reproducibly isolated without undue experimentation. Accordingly, filing of evidence of the reproducible production of the cell lines and antibodies necessary to practice the instant invention or filing of evidence of deposit is required. Without a publicly available deposit of the above cell lines, one of skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: the claimed cell line; the cell lines which produce the chemically and functionally distinct antibodies claimed; and/or, the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event. For example, very different V_H chains can combine with the same V_L chain to produce antibody binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_L sequences to produce antibodies with very similar properties. These observations indicate that divergent variable region sequences, both in and out of complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. Therefore, it would require undue experimentation to reproduce the claimed monoclonal antibody species chemically as produced by the hybridomas designated

FERM BP-7295 or FERM BP-7296. A suitable deposit of the hybridomas would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See the criteria set forth in 37 CFR §§ 1.801-1.809.

If the deposits are made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty, that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent and that the biological materials will be replaced should they ever become non-viable, would satisfy the deposit requirement made herein.

If the deposits have not been made under the Budapest Treaty, then in order to certify that the deposits meet the criteria set forth in 37 CFR §§ 1.801-1.809, applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposits will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) the deposits were viable at the time of deposit; and,

(e) the deposits will be replaced if they should ever become non-viable.

Claims 1-4 and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant does not provide description of or guidance to a method of separately measuring low molecular weight CD14 fragments in a sample other than by immunoassay and by

subtraction of determined measurements of total and high molecular weight CD14. In the absence of further written description and guidance from applicant, one would not be assured of measuring, if measuring encompasses direct measurement of low molecular weight CD14 fragments, in the absence of total and high molecular weight CD14 determinations.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "low molecular" and "high molecular" in claims 1, 2, 4-7, and 11-14 are relative terms which render the claim indefinite. The terms "low molecular" and "high molecular" are not defined by these claims, the specification does not provide a standard for ascertaining the requisite degree of "molecular", and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claims 1-3 and 14 are method claims and, as such, they should clearly set forth the various method steps in a positive, sequential manner using active tense verbs such as mixing, reacting, and detecting. Claims 1 and 3 are indefinite because without any active, positive steps delimiting how the method is actually practiced it is unclear what method/process applicant is intending to

encompass. The claims should also clearly state each component used in the method and the relationship of the various components, and should not be a mere recitation of a desired outcome. Method claims should also conclude with a step relating the method result to the purpose of the method, preferably to the purpose as also set forth in the preamble of the claim.

In claims 2, 3, and 14, "the total amount" and "the amount of high" lack antecedent basis.

In claims 5-8 and 11-14, "does not bind to no low" is vague as to what is encompassed or excluded.

In claim 6 and claims dependent thereupon, "the amino acid sequence" lacks antecedent basis. In these claims it is not clear what is encompassed because it is not clear if the antibody need only bind one of the listed 41 amino acid residues, or if the antibody binds to a C-terminal epitope within full length soluble CD14.

In claim 7 and claims dependent thereupon, "any one of the C-terminal", "the sequence", and "the" 316th, 328th, 331st, or 345th positions lack antecedent basis.

In claim 9, --produced by a hybridoma cell line deposited as Accession No. FERM BP-7295 or...-- would be clear as to what is intended.

In claim 10, "the sequence" and "the" 316th or 356th amino acids lack antecedent basis.

Claim 13 provides for the use of at least one antibody, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Method claims should also conclude with a step

relating the method result to the purpose of the method, preferably to the purpose as also set forth in the preamble of the claim. In this claim, "the quality or quantity" lacks antecedent basis.

In claim 14, --determining-- and --soluble-- should be recited. In this claim it is believed that applicant intended claim --13-- rather than claim "12." It is not clear what is being determined because it appears that applicant's intent is to have the claim depend upon two different method claims involving two different determinations.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 13 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 5-8 and 10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. There is no indication that the product(s) as claimed are isolated and no claimed degree of purity for the product(s) which would indicate "the hand of man". Thus, the products as claimed are considered a product of nature which is non-statutory subject matter.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 5, 10, 13, and 14 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Stelter et al. (Eur. J. Biochem 236: 457, 1996).

Stelter et al. teach antibodies that bind to soluble CD14 (sCD14) and the use of the antibodies to determine the relative amounts of high and low molecular weight CD14 proteins in samples, including from human serum (see e.g. Table 2). The reference teaches purified sCD14 which comprises the sequence of the polypeptide as claimed.

Claims 1, 4, 5, 10, and 13 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Landmann et al. (J. Inf. Dis. 171: 639, 1995).

Landmann et al. teach antibodies that bind to soluble CD14 (sCD14) and the use of the antibodies to determine the relative amounts of high and low molecular weight CD14 proteins in samples, including from human serum (see e.g. Fig. 3). The reference teaches purified sCD14 which comprises the sequence of the polypeptide as claimed.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 5-8 and 11 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Leturcq et al. (WO 94/28025).

Leturcq et al. teach immunization of mice with full length soluble CD14 and the elicitation of polyclonal and monoclonal antibodies. The antibodies of the reference appear to anticipate the antibodies as instantly claimed because one would have expected the elicitation of antibodies to any immunogenic epitope of the full length protein, particularly in the polyclonal antibody population, and the epitopes bound by the antibodies of the reference, polyclonal or monoclonal, cannot be determined from the disclosure therein. Further, the Patent and Trademark Office does not have the facilities and resources to provide the *factual* evidence needed in order to establish that there is a difference, in the first place, between the reagents of the prior art and those instantly disclosed and,

that if there is such a difference, that such a difference would have been considered unexpected, i.e. unobvious, by one of ordinary skill in the art. The burden is upon applicant to present such factual evidence. See e.g. In re Best (195 USPQ 430 (CCPA 1977)) or Ex parte Phillips (28 USPQ2d 1302 (BPAI 1993)).

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Ferrero et al. teach the sequence of CD14.

Grunwald et al. (J. Immunol. Meth. 155: 225, 1992) teach a sandwich ELISA for determination of soluble CD14.

Landmann et al. (Inf. Imm. 66: 2264, 1998) teach monoclonal antibodies to soluble CD14.

Lauener et al. (WO 96/32418) teach monoclonal antibodies to soluble CD14.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (703) 308-3980. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (703) 305-3399.

The phone numbers for official facsimile transmitted communications to TC 1600, Group 1640, are (703) 872-9306, or (703) 305-3014, or (703) 308-4242. Official After Final communications, only, can be facsimile transmitted to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. The above inquiries, or requests to supply missing elements from Office communications, can also be directed to the TC 1600 Customer Service Office at phone numbers (703) 308-0197 or (703) 308-0198.

James L. Grun, Ph.D.
October 22, 2003

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641